

Anti-interleukin-6 monoclonal antibody for cytokine storm in COVID-19

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Abstract:

Novel coronavirus disease 2019 (COVID-19) is known to cause severe pneumonia and acute respiratory distress syndrome which may lead to death. Several treatments have been tested in the race to find a treatment regimen for this deadly viral infection. Tocilizumab, a recombinant humanized anti-interleukin-6 receptor monoclonal antibody, has been used and found to be beneficial in patients with COVID-19 and in cytokine storm. We present the case of a young, otherwise healthy male, presenting with COVID-19 and successfully treated in the intensive care unit with tocilizumab.

Keywords:

COVID-19, cytokine, interleukin-6, infection, monoclonal antibody, tocilizumab

Novel coronavirus 2019 (COVID-19) has already caused over 4.5 million infections across 216 countries and accounted for over 300,000 deaths as of May 16, 2020.^[1] This viral infection is known to cause severe respiratory illness and produce a cytokine storm associated with increased morbidity and mortality.^[2,3] While several medication regimens have gained recognition and are being used to treat COVID-19, tocilizumab, a recombinant humanized anti-interleukin-6 receptor monoclonal antibody, has been found to be effective in managing the cytokine storm.^[4] We present the case of a young male diagnosed with COVID-19 infection with significant improvement of symptoms after receiving one dose of tocilizumab.

Case Report

A 42-year-old male physician with no medical history and in overall good health presented to the emergency department complaining of worsening dry cough, chills, and fevers of 101°–102° Fahrenheit for the past 6 days. He stated over the last

2–3 days; his symptoms were accompanied with severe shortness of breath worse on exertion. He denied any recent travel and stated his son was home sick from school with common cold-like symptoms. On admission, his blood pressure was 115.70 mm Hg, heart rate of 94 beats/min, temperature of 100.6°F, respiratory rate of 18 breaths/min, and oxygen saturation of 88%–89% on room air. Physical examination was significant for respiratory distress and diaphoresis. He was placed on a 2 L/min (LPM) nasal cannula, and a chest X-ray showed bilateral mid and lower lung zone airspace disease suggestive of pneumonia [Figure 1]. Azithromycin 500 mgs intravenously (IV) daily and ceftriaxone 1-gram IV daily were started. A viral respiratory panel and COVID-19 test through RT-PCR was obtained. The following day his respiratory status declined, and oxygen requirement increased. Due to severe anxiety and distress, he was placed on optiflow at 40 LPM and 40% fraction of inspired oxygen (FiO2) and transferred to the intensive care unit (ICU) for further monitoring. His viral respiratory panel and influenza A and B test were negative, and his COVID-19 test returned positive on day 3. Empiric therapy with 6 g of Vitamin

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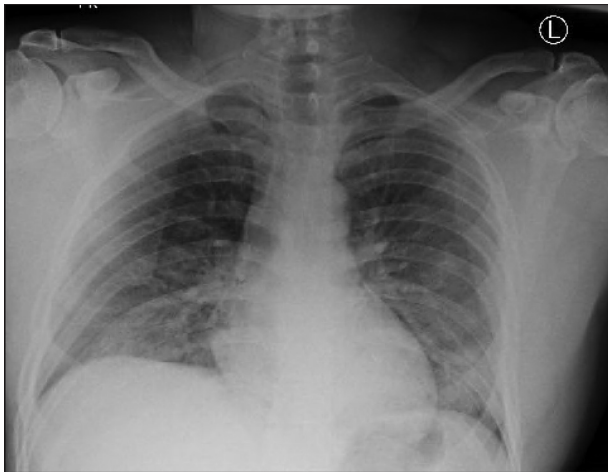


Figure 1: Chest X-ray bilateral mid and lower lung zone airspace disease with central greater than peripheral distribution suggestive of multifocal pneumonia. Superimposed bilateral parabrachial thickening

C twice daily, 400 mg hydroxychloroquine daily, 220 mg zinc sulfate daily, and continued on 500 mg azithromycin daily for a 5-day course. On day 3, his oxygen requirement increased again to 60% FiO₂ to maintain an oxygen saturation >92%. He remained with high-grade fevers of about 102° despite IV Tylenol administration. The decision was made to give 664 mg (8 mg/kg) of tocilizumab. By day 4, his temperature began to decrease, and his respiratory status improved. His oxygen requirement while in the ICU was titrated down, and by day 5, he was placed on high-flow nasal cannula at a rate of 10 LPM. He was transferred to the general medical floors for further monitoring and titration of supplemental oxygen requirement. On day 8, he was discharged home without the need of supplemental oxygen and in good health and advised to self-quarantine for 14 days.

Discussion

In COVID-19 infections, interleukin-6 (IL-6), IL-2R, IL-10, and tumor necrosis factor alpha are elevated and found to be associated with more severe disease.^[5] IL-6 is known to induce synthesis of acute-phase reactants and plays a role in antibody and T-cell maturity.^[6] With this overwhelming inflammatory response, IL-6 has been presumed to be the main culprit of the “cytokine storm” found in COVID-19 infection. Tocilizumab is a recombinant humanized anti-IL-6 receptor monoclonal antibody with an approved maximum dosage of 8 mg/kg intravenously.^[7,8] Since the 1990s, tocilizumab has been used to treat several immune-mediated diseases such as rheumatoid arthritis.^[6] With the notion in mind of impairing the damage done by the host-immune system and acute-phase reactants, tocilizumab has been used as an off-label treatment in COVID-19.^[4] In our patient presented, it was suspected the high-grade

fevers and sudden increase in oxygen requirement were due to a cytokine storm. After receiving tocilizumab, there was a significant improvement of symptoms, and the patient had a successful recovery. These findings are also supported by Luo *et al.*, although repeated doses of tocilizumab were needed for symptomatic improvement.^[9]

Tocilizumab has been shown to be of benefit in COVID-19-related cytokine storm and should be considered in these critically ill patients. However, caution should be noted with each tocilizumab dose. IL-6 is known to be a strong immunomodulator and when blocked with agents such as tocilizumab can lead to significant immunocompromise. This can lead to the patient being prone to infections, especially in the intensive care unit setting. It has also been found that decreasing IL-6 too early in the infection course can lead to an increased viral replication period leading to increased mortality.^[10]

Being defined as a pandemic by the World Health Organization in March 2020, the race for treatment guidelines and vaccinations has driven medical communities globally. While several treatments have shown promising results and patient outcomes, there is still not an approved management algorithm for COVID-19 infection. Tocilizumab studies are also lacking and clinical trials evaluating safety and efficacy are desperately needed.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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